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Arthrogryposis Associated With Unsuccessful Attempts at Termination of Pregnancy

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We report three cases of failed termination of pregnancy in which the children were subsequently born with arthrogryposis (AMC) (multiple congenital contractures). Arthrogryposis is a sign with many causes. We suggest that the multiple congenital contractures seen in these children are due to vascular compromise during the attempted termination with secondary loss of functional neurons leading to fetal akinesia and subsequent contractures. Two of the children have additional evidence of intrauterine vascular compromise. Limitation of movement secondary to the rupture of the fetal membranes and continuous leakage of amniotic fluid after the attempted termination may have compounded the contractures in two of the children. © 1996 Wiley-Liss, Inc.

KEY WORDS: arthrogryposis, termination of pregnancy, contractures, vascular

INTRODUCTION

Arthrogryposis multiplex congenita (AMC) is a term used for almost a century to describe conditions with nonprogressive congenital joint contractures. The conditions that have been described as arthrogryposis multiplex congenita range from well-known syndromes to nonspecific combinations of joint contractures [Hall, 1985]. The shorter term "arthrogryposis" is usually used to imply multiple joint involvement, and is most often reserved for nonprogressive conditions that involve more than one part of the body.

The exact pathogenesis of most cases of arthrogryposis is not known, but all involve decreased fetal movement (i.e., fetal akinesia). The suggested mechanisms for decreased fetal movement include: (1) abnormalities of nerve structure or function, including both central and peripheral nervous systems, (2) abnormalities of muscle structure or function, (3) abnormalities of connective tissue, (4) limitation of space or movement within the uterus, (5) intrauterine vascular compromise, and (6) maternal illness [Hall, 1985]. Once fetal akinesia occurs, contractures of the involved joints begin to develop. The longer the decrease of fetal movement, the more severe the limitation of joint movement and the more likely that extra connective tissue will be present around the joint.

The number of attempts at termination of a pregnancy that fail (i.e., the pregnancy continues) is estimated at 0.05% [Steier and Bergsjo, 1991]. Most of the cases of failed terminations [Achelis, 1950; Stadler and Hardt, 1976; Hardt et al., 1980; Hundsdorfer and Schultz, 1982; Lipson, 1989; Collins and Mahoney, 1991; Holmes, 1995] reported so far have been associated with limb or digit abnormalities and congenital contractures. However, it is likely there has been bias leading to the reporting of abnormal cases.

We report three well-documented cases of attempted termination of pregnancy in which the children were born subsequently with arthrogryposis and suggest that vascular compromise leading to loss of functional neurons with secondary decreased fetal movement is the cause of the contractures. Early amniotic rupture related to the procedure may have compounded some of the contractures but is unlikely to have been the primary cause of the multiple congenital contractures seen at birth in these individuals.

CLINICAL REPORTS

Patient 1

At the time of birth, the mother was 30 and the father 32 years old. Both parents were Caucasians of Belgian descent and are first cousins. The mother had one previous first trimester spontaneous abortion and one normal pregnancy resulting in a normal healthy son. The family history was noncontributory and nonsignificant except that the son developed testicular cancer. The mother's previous medical history was unremarkable.

Four weeks after her last menstrual period, the mother developed persistent vaginal bleeding that lasted 5–6 weeks. She consulted her physician who made a clinical diagnosis of incomplete miscarriage and performed di-

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Dedicated to Jürgen W. Spranger on the occasion of his 65th birthday with admiration and best wishes.

latation and curettage at ~8–10 weeks of gestation (estimated to be 10–12 weeks from last menstrual period). Pethidine and atropine were given as premedication for the curettage. No histology report was available from the D&C. Following the procedure, oral contraceptives were prescribed to bring on menstruation. Because her period had not resumed after 2 months and because she was experiencing nausea, vomiting, and an enlarging abdomen, she discontinued the oral contraceptives. Ultrasound studies done 21 weeks after her last menstrual period confirmed that she had an ongoing pregnancy. The remainder of the pregnancy was uneventful. The pregnancy ended at 32 weeks when a caesarean section was performed due to a very painful and distended uterus thought to be consistent with abruptio placentae and transverse lie position. A placental mass was noted at birth and histopathological examination reported a mature placenta with a large subchorionic and intravillous haematoma. Numerous small fibrotic placental villi were found in the mass. The pathology report concluded that the mass was the result of massive intravenous fibrous thrombosis and old haemorrhage due to the failed curettage.

Birth. Birth weight was 1.26 kg (25th centile for 32 weeks), length 47.3 cm (95th centile for 32 weeks), and OFC was 29.5 cm (25th centile for 32 weeks). Peripheral pulmonic stenosis was noted at birth. She was hirsute and said to have a "myopathic face" with puffy eyelids. She had a depressed bridge of the nose, micrognathia, high palate, and unfolded ears. Limb contractures included equinovarus feet, stiffness of the lower limbs, extended and fixed left knee, dislocated hips, and short right leg. She had a scar on her leg behind her right knee. Biochemical screen and chromosomes were normal. She did well neonatally except for a period of hyperbilirubinaemia, which was treated with phototherapy and a period of respiratory distress that resolved spontaneously. She fed well and her neurological development was normal. Since birth she has had numerous operations to correct the contractures, but has otherwise been well.

Physical examination. At 16 years, she was a pleasant, cooperative girl (Fig. 1). Her weight was 50 kg, her height 155 cm. She had nasal speech. She had a mildly "myopathic" face with prominent eyes that did not close completely and could be opened easily by the examiner when she was trying to keep them closed. She had bilateral ptosis, mild micrognathia, difficulty in completely opening her mouth, and a short high arched palate. She had restriction of movement at her right hip, extended knees (could not be flexed beyond 20–30°) bilaterally, and small patellae. Her right leg was 1.5 cm shorter than her left. She had dimples around her knees. She had pes cavus and tight Achilles tendons bilaterally. She had bilateral camptodactyly of the 2nd and 5th fingers as well as mild cutaneous syndactyly of all fingers particularly on the left hand (Fig. 2). She was mildly hirsute and had a slightly low posterior hair line. She stood with increased lumbar lordosis. There was a smooth hairless depression (like a scar) running along on the back of the right knee (Fig. 3) and a small sacral dimple. At present she is a student in high school, she is lefthanded, her intelligence is normal, and she walks without aides.

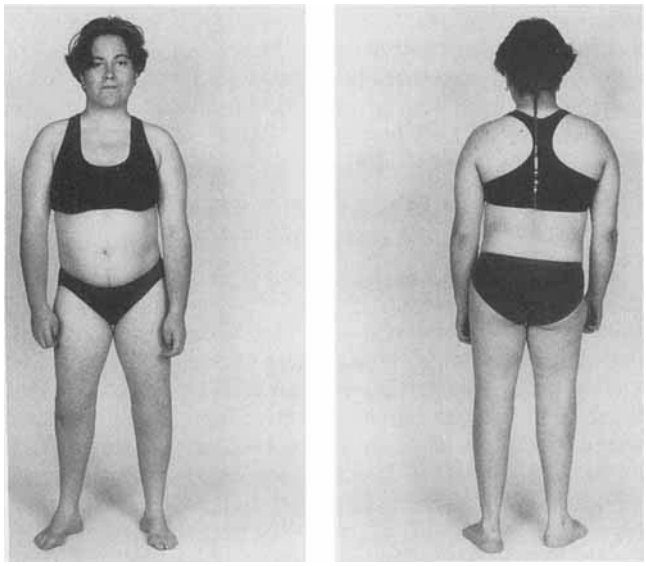

Fig. 1. Patient 1 at 16 years.

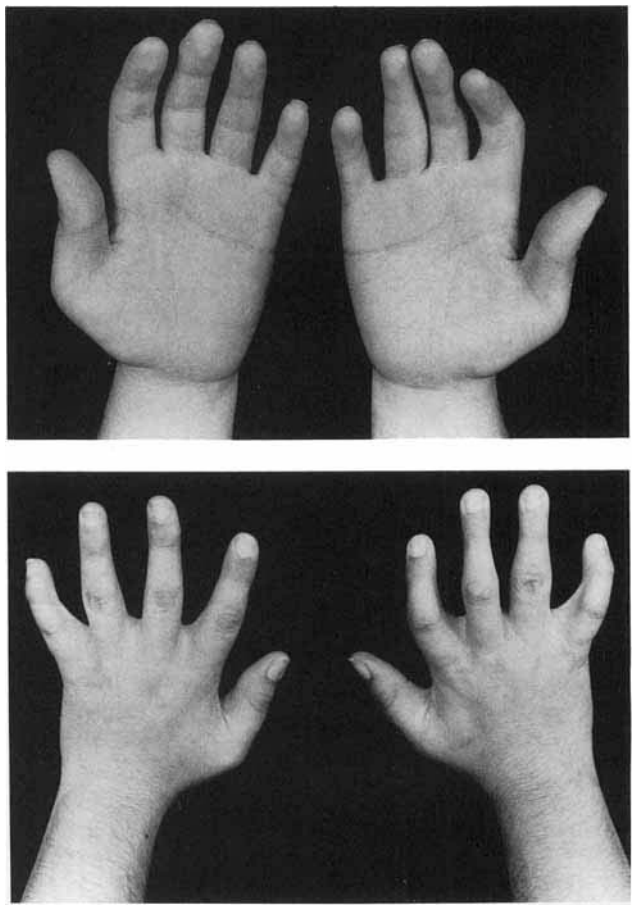

Fig. 2. Hands of patient 1 at 16 years.

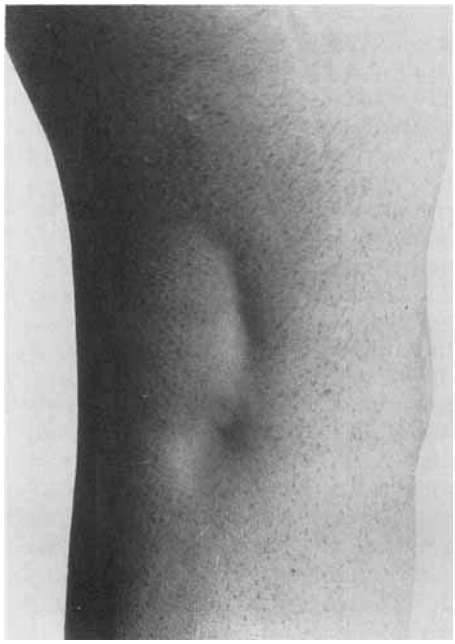

Fig. 3. Back of the right leg of patient 1 at 16 years.

Patient 2

The mother was 26 years old at the time of birth, the father 28. They were nonconsanguineous. Both were Caucasian of European descent, and this was the mother's third pregnancy. The first pregnancy was uncomplicated and ended with the delivery of a healthy female; the second pregnancy was a first trimester spontaneous abortion. The family history and the mother's medical history were unremarkable. At 10 weeks after the date of last menstrual period (i.e., 8 weeks gestation), the mother had several episodes of heavy bleeding and cramping with passage of blood clots. A clinical diagnosis of incomplete abortion was made and a D&C was performed. The pathology report documented fragments of haemorrhagic and necrotic decidual tissue, but no chorionic villi. Four weeks after the D&C, she noted leakage of clear liquid. This was interpreted as a urinary tract infection and was treated with antibiotics. The mother was told that the medication would color her urine green. During the treatment the urine did change color, but the clear liquid leakage continued. Six weeks after the D&C, Norlutate® (1 daily) was prescribed to resume her menstrual periods. She visited her physician once more after finishing the Norlutate and still had no menstruation. At 18 weeks after her LMP (i.e., 16 weeks gestation), an ultrasound study confirmed an ongoing pregnancy of ~15–16 weeks. The vaginal clear liquid leakage continued sporadically throughout the remainder of the pregnancy. The leakage was significant, the mother referred to it as "—a fantastic amount of liquid that poured down her legs, would wet her slacks, and make puddles on the floor—." She suggested that she was leaking at least 2 cups a day and particularly every time she felt the child move. The pregnancy ended with a normal vaginal delivery at 32 weeks. The placenta was said to be normal with two vessels and no amniotic bands were described.

Birth. Birthweight of this boy was 1531 g (<10th centile for 32 weeks); birth length and OFC were not recorded. At birth there was hirsutism of back and face, a strawberry haemangioma of the back of the neck, and a cavernous haemangioma over the right posterior chest. His upper limbs were small. The left arm was shorter than the right. His left elbow was extended with decreased muscle mass of the left forearm and a hyperextended left wrist. He had dislocated hips, flexed knees, and dorsiflexed feet. He had a left abdominal wall muscular defect. He had multiple areas of atresia of the bowel and required a colostomy in the newborn period with later resection. He has had multiple castings and braces to correct his contractures.

Physical examination. At the age of 7 years, the boy was pleasant, small, and thin (Fig. 4). Head and face were normal with mild esotropia, normal jaw opening, and numerous repaired cavities. He had very strong upper trunk muscles and slightly prominent vessels over his chest wall. His chest had a decreased AP diameter. His lower body appeared small. His right arm was normal. The left forearm was short with decreased muscle mass. It lacked complete supination, and there was mild hyperextensibility of the wrist and fingers. His left hand was smaller than his right and the thumb was proximally placed. He had clinodactyly of the 5th finger bilaterally but more so in the left hand. The hand creases were present but with different angles on each hand. He had a faint strawberry haemangioma on his neck and a resolved cavernous haemangioma over the right posterior chest. He had a defect of the left abdominal wall muscle and fascia below the edge of the rib. He had small hips, extended fixed knees, fixed ankles, and plantigrade feet. He had had extensive surgeries to correct his contractions and walked with the aid of crutches. At present, he is 22

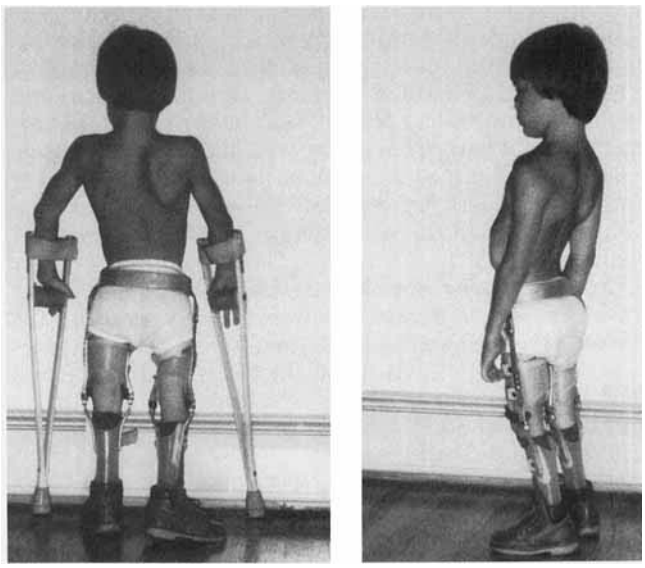

Fig. 4. Patient 2 at 7 years.

years old. He attends college, holds a clerical job, lives independently, and has normal intelligence. He continues to walk with the aid of braces and crutches and occasionally uses a wheelchair.

Patient 3

The mother was 33 years old at the time of birth; the father was 30. She had occasionally used "recreational drugs" before the pregnancy. This was her first pregnancy, and it was unplanned. The family history was noncontributory, although the father had mild ptosis and the mother's brother was slow in motor development but had done well as an adult. Mother had had recurrent genital herpes treated with Acyclovir prior to the pregnancy and during the pregnancy at 12 and 28 weeks.

At ~13–14 weeks (i.e., 11–12 weeks gestation) after her last menstrual period, a therapeutic abortion was performed. Six weeks after the abortion, the mother had not resumed her menstrual period and noted weight gain as well as continuous clear vaginal fluid discharge. An ultrasound scan was performed at this time (20 weeks after last menstrual period, thought to be 18 weeks gestation) and showed a fetus with varying measurements between 19 and 23 weeks in a breech presentation with moderate to severe oligohydramnios. At 21 weeks, endometritis and herpes vulvitis were diagnosed. At 25 weeks, the membranes ruptured spontaneously. At 29 weeks, another ultrasound study documented severe oligohydramnios. At 30 weeks, she had recurrence of herpes vulvitis and was treated with Acyclovir. At 31 weeks, she started spontaneous labor, and a caesarean section was performed due to breech presentation and the presence of herpes. No abnormalities of the placenta were noted.

Birth. Birth weight of this girl was 1,590 g (50th centile for 32 weeks), length 38 cm (10th centile for 32 weeks), and OFC was 29.3 (25th centile for 32 weeks). The neonatal period was complicated. The Apgar scores were 5, 7, and 10 at 1, 5, and 10 minutes; bag and mask resuscitation were necessary and she was hypotonic. She was hirsute, had frontal bossing, and a small nose with anteverted nares. During the neonatal period, she had intermittent jaundice, hyaline membrane disease, and necrotizing enterocolitis that required partial colectomy and terminal ilectomy. In addition, she had hypertelorism, esotropia, frontal bossing, and apparently low-set ears. There was overall decreased muscle mass with significant short of left upper and lower limbs, flexed left hip and left knee, bilateral equinovarus. She had mild webbing of the axillae and popliteal area.

During infancy she had developmental delay and was diagnosed with spastic cerebral palsy secondary to perinatal hypoxia ischemic injury. TORCH testing was negative. An MRI of the head showed mild dilatation of ventricles and generous subarachnoid space. Muscle biopsy showed mild fibre disproportion. MRI of the muscles showed mild atrophy.

Physical examination. At the age of 6 years, she had developed into a pleasant, slender girl in a wheelchair. She had frontal bossing, depressed nasal bridge, small nose with anteverted nostrils, long philtrum, hypoplastic malar areas, and retrognathia. She had slight pectus excavatum and a funnel-shape chest. She had one café-au-lait spot on the right lower quadrant of the abdomen and another one in her right inguinal area. She also had some irregular linear pigment on her right arm. Her lower limbs were spastic and hypotonic; she had flexion contractures of the left hip and both knees, tight heel cords and rocker bottom feet. Her gluteal areas are hypoplastic, she had thoracic kyphosis, scoliosis, and mild left hemiparesis. She had mild webbing of the neck, axillae, and popliteal area. Her proximal and distal interphalangeal digits are hyperextensible, and she had single transverse palmar creases bilaterally. She had continuous problems with wound healing and had developed a granuloma annulare of the right ankle, which has responded to steroid treatment. She has soft skin, wide scars, and mild hyperextensibility. A blind pouch separating the vagina from the rectum was repaired surgically. She was developmentally delayed functioning at a mental age of ~3 years 2 months.

At present she is 11 years old, has very poor muscle development, and gets around in a wheelchair or with braces. An MRI scan demonstrated generalized mild atrophy of the muscles in and around the thighs and pelvis. She is developmentally delayed and is currently in grade 3 but requires an individual aid.

DISCUSSION

The first studies of failed terminations of pregnancies after an attempted abortion were reported in the early 1970s and reviewed the results of menstrual extraction [Brenner et al., 1973]. They reported a failure rate between 1.1 and 4.2% for menstrual extractions. Brenner et al. [1973] also noted that the frequency of failures decreased as pregnancy duration increased.

In 1978, Fielding et al. [1978] studied a much larger population, reporting on 65,045 surgical terminations of pregnancy performed at 5 centres over a period of 100 months; 46 of the women documented had failed to achieve an abortion, i.e., the pregnancies continued. The incidence of failed abortions from this large group of D&Cs was 0.071% or 1 in every 1,414 abortions performed. The gestational age of the pregnancies (dated from the date of last menstrual period) that continued varied; 75% were 8 weeks or less and the rest were 6 weeks or less. Of the continuing pregnancies, 97% were eventually terminated with another procedure or miscarried. Only one woman chose to continue with her pregnancy and delivered a normal unaffected infant.

More recent studies have continued to estimate the number of attempts at termination of a pregnancy that fail at ~0.05% [Steier and Bergsjo, 1992]. Most of the single case reports of failed terminations [Collins and Mahoney, 1983; Lipson and Webster, 1993] have been associated with limb or digit abnormalities and congenital contractures. However, a recent report describe two cases with craniofacial anomalies [Holmes, 1995].

Studies on animals [Chernoff and Gyabowski, 1971; Kennedy and Persaud, 1977; Leist and Grauwiler, 1974; Webster et al., 1987] have shown that handling of the pregnant uterus disturbs uterine blood flow and results in temporary hypoxia and bradycardia of the em-

bryo/fetus. These changes may be associated with limb deficiencies, limb contractures or miscarriage.

Danielson et al. [1992] reported that some vasodilating drugs such as nifedipine, nitredipine, felodipine and hydralazine are associated with digital defects in rabbits. The defects observed in the rabbits were absence, abnormal structure or fusion of the distal phalanges. The dose, timing, and duration of the vascular insult during embryogenesis were critical. Increasing doses of vasodilating drugs were directly related to the severity of the malformation. The timing (gestational age) and duration of the drug exposure were associated with specific malformations in rabbits.

Horoupian and Yoon [1988], Reid et al. [1986], Robertson et al. [1994] have suggested that in human embryogenesis, neuronal destruction secondary to ischemic event during a critical period in the development of anterior horn cells may result in congenital contractures presumedly due to disruption or decreased flow in the anterior spinal arteries and damage to the developing anterior horn cells and secondary lack of normal fetal movement resulting in congenital contractures. The additional congenital anomalies seen in Patients 1 and 2 could have been the result of decreased vascular flow or an obstruction in vascular flow leading to necrosis of skin, muscle layers, and bowel.

Additional evidence for the role of vascular compromise in the pathogenesis of contractures and congenital anomalies in humans has been reported associated with prenatal chorionic villus sampling, selective termination or reduction of numbers of fetuses in multifetal pregnancies, and cocaine use during pregnancy.

Chorionic villus sampling (CVS) is a procedure by which a sample of the chorionic villi of the placenta is taken at ~10–11 weeks of gestation. The purpose of CVS in most cases is to do early prenatal testing for genetic disorders. Several authors have suggested that CVS inflicts a vascular insult to the placenta that results in hemorrhages or decreased uterine blood flow that disrupt the early development of the embryo's limbs particularly distally [Firth et al., 1991; Brambati et al., 1992; Schloo et al., 1992]. However, reported cases have not usually had arthrogryposis.

Recent reports also have suggested that transverse limb deficiency and oro-mandibular limb hypogenesis (Hanhart) sequence may be related to chorionic villus sampling particularly if performed during days 56 and 66 of gestation [Firth et al., 1991; Froster and Baird, 1992]. Möbius syndrome may be seen with oro-mandibular hypogenesis and multiple congenital contractures and also has been associated with an intrauterine vascular pathogenesis [Lipson et al., 1989; Lipson and Webster, 1993].

Selective termination or reduction of the number of fetuses has been performed in multifetal pregnancies resulting from ovulation induction techniques or to prevent the birth of a fetus with congenital abnormalities while allowing an unaffected fetus to continue its pregnancy [Golbus et al., 1988]. There are a number of different techniques to perform selective termination including: air insufflation [Rodeck et al., 1982], fetal exsanguination, transcervical aspiration [Dumez and Oury, 1989], injection of potassium chloride [Wapner et al., 1990], and hysterotomy [Golbus et al., 1988]. Regardless of the technique, short-term complications are rare; however, transvaginal reduction of number of fetuses carries a significant risk of spontaneous loss of the remaining fetus(es). Selective reduction of fetus(es) potentially puts the remaining fetus(es) at risk for vascular compromise, particularly if vascular connections exist between the fetuses and their placentae.

More evidence for the role of vascular compromise in the mother and the developing embryo/fetus has been reported with the use of cocaine during pregnancy. The use of cocaine during pregnancy is known to lead to placental hemorrhages, abruptio placentae, fetal death [Acker et al., 1983], intrauterine growth retardation [Handler et al., 1991], and/or fetal malformations [Chavez et al., 1989].

There have been reports of failed curettage abortions [Achelis, 1950; Stadler and Hardt, 1976; Hardt et al., 1980; Hundsdorfer et al., 1982; Collins and Mahoney, 1983; Lipson et al., 1993; Holmes, 1995] (Table I) in which the children were born with a variety of congenital anomalies. One case of failed abortion by curettage was also documented [Lipson and Webster, 1993] to have Möbius syndrome (congenital seventh nerve palsy, unilateral or bilateral associated with other cranial nerve palsies and/or musculoskeletal abnormalities).

There is a number of potential mechanism by which vascular compromise could cause congenital contractures. A decrease in the blood flow due to decreased uterine vessel flow or due to placental vascular compromise may lead to hypoxia or anoxia, which could then lead to damage and/or loss of the neurons and/or muscles. Handling the uterus apparently leads to vascular constriction and secondary decrease in placental flow. Compromised or slow flow of blood also may lead to the formation of a clot and blockage of circulation. Direct damage and/or anoxic damage to tissues may occur if there has been obstruction of blood flow. Tissue fragments or tissue extracts leading to clotting or vasoconstriction could also potentially block or decrease circulation. It is likely that tissue sensitivity to hypoxia and anoxia vary depending on the tissue type and time in development. We hypothesize that the anterior horn cells are particularly susceptible to hypoxic damage and/or loss in early fetal development (i.e., 8–14 weeks of gestation).

Among monozygotic (MZ) twins coming to term, 70% share vascular connections through their placenta [Machin, 1996]. MZ twins are known to be at increased risk for congenital anomalies particularly of the vascular type. Reports of vanishing twins suggest that up to 70% of twin pregnancies spontaneously convert to singletons or abort [Jeanty et al., 1981; Jauniaux et al., 1986]. It has been suggested that vascular compromise plays a very important role in that loss, as well as in the congenital anomalies seen in surviving MZ twins. MZ twinning is seen with increased frequency among the amyoplasia type of arthrogryposis in which only one twin is affected [Hall et al., 1983]. The cases in the present report do not have amyoplasia, nor was there any suggestion of a twin on examination of the placentae.

TABLE I. Review of Reports of Individuals Born After Attempted Terminations of Pregnancy in the Literature

Case no.	Procedure	Week of gestation	Anomalies	Reference
1	Curettage	Unknown	Anophthalmia	Achelis, 1950
2	Curettage	Unknown	Missing left arm	Stadler and Hardt, 1976
3	Unknown	Unknown	Abnormal	Hardt et al., 1980
4	Unknown	Unknown	Meningomyelocele	Hundsdorfer and Schultz, 1982
5	Unknown	Unknown	Möbius sequence	Lipson et al., 1989
6	Intramniotic injection of prostaglandins	7	Hydrocephaly, abnormal digits	Collins and Mahoney, 1983
7	D&C	8	Hydrocephaly, facial cleft, IUGR, scalp defects, constriction rings 4th finger, gyral brain pattern abnormality	Holmes, 1995
8	D&C, air insufflation, and hysterosalpingography	6	Scalp defects hypertelorism, low set ears, scoliosis, right preauricular tag	Holmes, 1995

Consideration was given to the possibility that the threatened abortion seen in each case associated with bleeding had actually been a miscarried twin, but no evidence to that effect was found.

Other authors [Shepard et al., 1991; Yu, 1991; Cohen, 1990] have suggested that amnion rupture during CVS may be the cause of the congenital contractures. Prolonged premature rupture of membranes (PROM) occurs in 2–3% of pregnancies. These authors suggest that the mechanical teratogenesis due to amniotic bands associated with PROM may lead to facial clefts and cerebral malformations and that the amniotic bands may limit movement. The congenital anomalies seen in Patient 2, in which there is a suspicion of early rupture of the amniotic membranes and chronic amniotic fluid leakage after the failed termination would fit such an association. However, no bands or evidence of amniotic bands were described at birth in Patient 2.

Oligohydramnios is present when there is less than the normal amount of amniotic fluid in the uterus during the pregnancy as was seen near delivery in Patient 3. Oligohydramnios often may be detected by ultrasound examination. When oligohydramnios is present fetal movements may be limited with subsequent development of congenital contractures. There are many causes of oligohydramnios, however, leakage of amniotic fluid from premature rupture of membranes or due to direct insult to the uterus during the pregnancy are certainly recognized to be associated with congenital contractures [Palacios and Rodriguez, 1990]. The contractures usually involve the large proximal joints symmetrically, with involvement of the more distal joints to a lesser extent. It is thought that oligohydramnios must be present for 3–4 weeks in order to produce contractures.

There are a number of common manifestations in the 3 case reports (see Table II): (1) all three had an attempted termination during early fetal life (~8–12 weeks of gestation), (2) all were delivered prematurely at 31–32 weeks, (3) all were small for gestational age,

TABLE II. Three Cases of Arthrogryposis after Failed Attempted Termination of Pregnancy

Patients	Procedure	Estimated weeks of gestation/delivery/placenta	Manifestations
Case 1 M-30_y F-32_y cousins $G_3P_1A_1$	D&C	8–10 weeks Delivery: 32 weeks by C section Placenta: large fibrous thrombosis	25th centile birth weight, peripheral pulmonic stenosis, hirsute with low posterior hair line, "myopathic" face, prominent eyes, bilateral ptosis, high arched palate, mild limitation of jaw opening, lumbar lordosis, right leg shorter than left, restriction of movement of right hip, extended knees, pes cavus, equine varus feet bilaterally, mild syndactyly of fingers, smooth scar on the back of right leg, normal intelligence.
Case 2 M-28_y F 32_y $G_3P_1A_1$	D&C	8–10 weeks; fluid leakage Delivery: 32 weeks, vaginal Placenta: normal but 2 vessel cord	10th centile birth weight, hirsutism, hemangiomas on the back of neck and right posterior chest, small upper limbs, left arm shorter than right, decreased muscle mass of the left forearm, hyperextended left wrist, dislocated hips, flexed knees, dorsiflexed feet, left abdominal wall defect, bowel atresias, normal intelligence.
Case 3 M-33_y F 30 G_1P_1Ao	D&C	11–12 weeks; genital herpes 29 weeks: ROM and oligo-hydrdramnios Delivery: 31 weeks by C section Placenta: apparently normal	10th centile birth length, 50th centile birth weight, hyoptonic hirsutism, frontal bossing, hypertelorism, esotropia, small nose, anteverted nares, low set ears, overall muscle mass decrease, myopathic facies, short left upper and lower limbs, webbing of the axillae and the popliteal area, flexed left hip and knee, bilateral neonatal jaundice, bilateral equinovarus, hyaline membrane disease, necrotizing enterocolitis leading to colectomy, unusual skin reactions with hyperextensibility, moderate mental retardation.

(4) all had upper limbs that were less involved than the lower limbs, (5) all had asymmetry of limb involvement, (6) all had hirsutism to some extent, (7) two had amniotic fluid leakage, (8) two had anomalies likely to be due to vascular compromise (the scar in Patient 1 and abdominal wall defects and bowel atresia in Patient 2), (9) two have "myopathic" or decreased facial movement, and (10) two are doing surprisingly well, whereas Patient 3 has moderate mental retardation but had a very complicated neonatal course and probably had the attempted termination at a slightly later time in pregnancy than the other two cases.

In spite of many complicating factors it seems likely that the congenital contractures seen in the three cases reported here are due to vascular compromise at the time of the attempted termination of pregnancy. Vascular compromise can be expected because of the anticipated decreased blood flow to uterine and/or placental blood vessels as well as the possible loss of placental vasculature related to the attempted termination of pregnancy. This decreased blood flow would be expected to result in fetal hypoxia. Vascular compromise giving hypoxia or anoxia within the fetus could be expected to lead to anoxic injury of tissue and/or to blood clots or blockage of blood flow also resulting in anoxia and possible cell death. The developing spinal cord and anterior horn cells are likely to be susceptible to anoxia in such a way as to lead to anterior horn cell death or failure of those neurons to mature normally. Lack of normal anterior horn cell function would be expected to lead to fetal akinesia and secondarily, multiple joint contractures. In summary, the congenital contractures seen in our three cases of failure of termination of pregnancy are most likely to be the result of a neuronal problem secondary to vascular compromise.

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